economic model with ten key parameters to calculate the ICERs associated with various combinations of inputs. Published HTAs were reviewed to determine the model inputs. Extensive scenario and multiway sensitivity analyses were carried out to document informative patterns and relationships between parameters that affected the results. **RESULTS:** Results showed that cancer sub-types with higher post-progression costs reduced a treatments likelihood of being cost-effective. The results also highlighted specific thresholds at which various cancer-specific case studies or combinations of inputs, including drug price, resulted in the drug being deemed not cost-effective using a threshold of £20,000 per QALY. **CONCLUSIONS:** The impact of post-progression costs can vary dependent on how these costs are modelled and also dependent on several factors, namely the ratios between health state utilities, 'background' costs, drug costs and the relative time spent in the stable and progressed disease states. It is demonstrated that, for many oncology treatments whose primary aim is to extend survival, this impact can be prohibitive to an intervention's probability of being cost-effective.

PRM112

DOSE-RESPONSE NETWORK META-ANALYSIS TO ADDRESS DOSE HETEROGENEITY IN A COST-EFFECTIVENESS ANALYSIS IN ACUTE MIGRAINE

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OBJECTIVES: Network Meta Analyses (NMAs) are often used to parameterise efficacy in decision models for economic evaluation. A common source of heterogeneity in NMA arises from the fact that treatments may be given at different doses. This variation may manifest as unexplained heterogeneity in standard NMA models and propagates through to the decision analysis. We aim to explore how dose-response NMA can be used to inform cost-effectiveness analysis using a cost-utility analysis of treatments for acute migraine. **METHODS:** We conducted four NMAs with different assumptions around dose-response to inform an economic evaluation in acute migraine. Separate 1-level NMAs were conducted where interventions were 'lumped' at the 'dose', 'treatment' and 'class' levels and a multi-level NMA was conducted, assuming monotonic dose-response. All NMAs were used to inform effect sizes in an economic model; the model structure, costing methods and utility inputs from the NICE Headaches guideline were adopted. The NMA models were compared in terms of heterogeneity and Deviance Information Criteria (DIC). We report the results of the economic analyses using cost-effectiveness acceptability frontiers (CEAFs). **RESULTS:** Dose-response parameterisation lead to NMA models with lower heterogeneity and better fit. Different dose-response parameterisations substantially changed the resource allocation decision, particularly at lower willingness to pay thresholds. For the more complex NMA model, it is unclear from a decision making perspective which effect size estimates should be selected as inputs to the decision model and we show that careful consideration should be given to the relevance of individual doses and confounding bias. **CONCLUSIONS:** Dose-response NMA provides a useful and arguably more appropriate method for conducting NMA for decision analysis. Careful consideration should be given to how to treat doses of the same intervention in NMA since different parameterisations may lead to biased effect sizes and sub-optimal conclusions around cost-effectiveness.

PRM113

IMPACT OF INTERNATIONAL AND THERAPEUTIC REFERENCING ON PRICES AND LAUNCH OPTIMIZATION

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OBJECTIVES: Majority of established pharmaceutical markets use pricing rules that reference products both across (international reference pricing; IRP) and within (therapeutic reference pricing; TRP) country-lines. Some markets, such as the UK, use no such rules and freely price therapies. IRP and TRP are used as effective measures to control price of pharmaceutical products. However, understanding the impact on a global level is considered highly complex, due to each market using different legislations and mechanisms. There is a growing need to better understand the impact of IRP and TRP on the decay of pharmaceutical drug prices and their effects on launch prices and sequencing across multiple markets. **METHODS:** We utilized a model to simulate the impact of IRP and TRP, as well as parallel trade, to quantitatively assess impact on drug prices across 40 markets (EU28, Switzerland, Russia, Iceland, Norway, Turkey, Israel, Brazil, Japan, South Korea, Australia, Canada and USA). The model uses simulating annealing parameters to also yield optimized launch sequences in all markets. **RESULTS:** Outputs of the model include impact to volume, price and revenue as well as parallel trade. Using a dynamic launch map, the model provides optimized price and launch sequence of a given pharmaceutical product. Within a set window, the launch and reimbursement dates were optimized based on a divergent set of rules and country baskets, often differing from manufacturers expected launch prices and sequences. While manufacturers are often able to secure higher price for therapies in free-price markets, the model clearly demonstrates the spill-over impact of referencing (both formally and informally) across countries and within therapeutic groups. **CONCLUSIONS:** Previously, launch sequences were optimized based on the implications on major markets. However, an expansive model looking at large number of markets that employ varying IRP and TRP rules will assist manufacturers in identifying an optimized price and launch sequence strategy.

PRM114

MODELING DISEASE PROGRESSION IN ALZHEIMER'S DEMENTIA TO INFORM HTA (CEA)

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OBJECTIVES: Alzheimer's dementia (AD) poses a significant challenge to health care systems around the world. Whilst treatment options are currently limited, with no effective disease modifying treatment, new advances in diagnosis and management of AD and promising advances in health technologies have the potential to significantly impact on the burden of the disease. However, alongside treatment advances it is important to improve the evaluation framework if we are to capture the potential benefits to people with AD. Methods to model disease progression over time, for use in comparative and cost-effectiveness analyses (CEA), is a priority area for further research. The objective in this research is to develop a new framework for modeling AD progression over time using the three main symptom domains of cognitive function, behaviour and mood, and functioning. **METHODS:** Development of a descriptive system, comprising a set of health states for AD, using the three symptom domains. Statistical modeling of disease progression through states over time, using US data from the National Alzheimer's Coordinating Center (NACC) (n=3009). The model is tested in a decision-analytic context, using time to progression and a cost-per-QALY framework. **RESULTS:** A 20-state disease progression pathway has been developed using multi-variate health states described using the three symptom domains. Transition probabilities and hazard rates have been estimated to model progression over time through the multi-variate descriptive system. In a baseline model over a 5-year timeframe, using mild-to-moderate AD starting states, 78% of people progressed to health states considered severe on at least one of the symptoms (46% severe for cognition). In a HTA context simulating a treatment with a modest effect the modeling framework predicted significant QALY differences between control and treatment over 5-years. **CONCLUSIONS:** This new modeling framework shows promise and presents a broader opportunity to capture the impacts of treatment over time using a range of symptom domains.

PRM115

USE OF EXTERNAL DATA TO GUIDE LONG-TERM SURVIVAL EXTRAPOLATIONS OF TRIAL DATA FOR CHRONIC LYMPHOCYTIC LEUKEMIA

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OBJECTIVES: The National Institute for Health and Care Excellence recommends utilising external data to evaluate the validity of extrapolation beyond trial follow-up. The objective was to demonstrate the use of external data to guide long-term survival predictions where only short-term trial data are available. **METHODS:** Four-year patient-level data for chlorambucil and ofatumumab+chlorambucil from the COMPLEMENT-1 trial were available; the survival rate was over 70% at four years. Published 18-year Kaplan-Meier data for chlorambucil from the C9011 study, which compared fludarabine and chlorambucil, were used to simulate a patient-level dataset. These data were not used directly as outcomes have improved substantially since patients were enrolled (1990-1994) and the chlorambucil dosing regimens differed. However the curve was used to guide the extrapolation of the COMPLEMENT-1 data using a three-stage approach: 1) Survival functions were fitted for the COMPLEMENT-1 and C9011 chlorambucil arms with an indicator for study. 2) The average treatment effect (chlorambucil versus ofatumumab+chlorambucil) was estimated from survival analysis for both arms of COMPLEMENT-1 and the C9011 chlorambucil arm, with indicators for treatment and study. 3) For ofatumumab+chlorambucil, long-term survival was estimated by applying the treatment effect from stage 2 to the function for chlorambucil from stage 1. Exponential, gamma, Weibull, log-normal, log-logistic and Gompertz functions were fitted. **RESULTS:** Weibull, Gompertz, and gamma functions provided reasonable fits during trial follow-up and plausible extrapolations (assessed by Akaike information criterion, Bayesian information criterion, graphical diagnostics, and expert clinical opinion). Survival predictions were markedly lower than conventional functions fitted to COMPLEMENT-1 data only (e.g. Weibull predictions for chlorambucil at 20 years were 8% vs 26%, respectively). **CONCLUSIONS:** Using long-term external data to guide the extrapolation provided plausible predictions for chlorambucil upon which alternative scenarios for the continuation of treatment effect observed in COMPLEMENT-1 could be explored.

PRM116

MODELLING EVOLVING CANCER RISK DURING EPIDEMIOLOGICAL TRANSITION USING ECONOMIC DATA

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OBJECTIVES: Epidemiological projections sizing patient populations are fundamental to budget impact analyses and market forecasting. When disease risk evolves over time, as in the case of epidemiological transition, using historical estimates in epidemiological projection becomes unjustified. Incorporation of additional variables that model evolving risk may allow for more reliable forecasts. The hypothesis that gross domestic product per capita (GDP) is correlated with disease risk was tested for a variety of cancers using global epidemiological and economic datasets. **METHODS:** Age-standardized incidence for 18 cancer sites across 188 countries was retrieved from the International Agency for Research against Cancer for the years 1993-1997. Corresponding country-specific GDP data was collected from the World Bank. For each site, correlation between GDP and incidence was measured using $R^2$and linear co-efficient values. **RESULTS:** Risk is strongly correlated with GDP for all of the sites studied, with the exception of the stomach (R^2=0; p>0.05). Correlation was strongest for those sites associated with diet/lifestyle factors prevalent in higher-income countries, namely: colorectal (R^2=0.61; p<0.001), breast (R^2=0.61; p<0.001) and lung (R^2=0.42; p<0.001). Strong association was also seen for prostate (R^2=0.47; p<0.001), although this may be explained by better case-detection in higher-income countries. Conversely, those cancer sites associated with infection showed a negative correlation, namely: cervix (R^2=0.33; p<0.01), liver (R^2=0.09; p<0.001) and oesophagus (R^2=0.06; p<0.01). **CONCLUSIONS:** GDP is strongly associated with cancer risk and varies by organ site in a manner concordant with the evolving exposures to known pathogens that characterize epidemiological transition. On the assumption that such correlation is a marker for various causal relationships, and that robust economic methods underlie GDP forecasts, it is reasonable to conclude that these correlations could be used to make epidemiological projections more accurate than projections assuming constant disease risk.